REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons which follow.

Introduction

Claims 1, 2, 4-11, 13 and 14 are pending in the instant application. Applicants confirm withdrawal of the previous rejection of claims 1-15 under 35 U.S.C. § 112, second paragraph.

Applicants have amended claims 1 and 11 to add a step for effectuating acylation reaction of a mixture obtained from a previous step, and to replace "more than 1 M of salts" with "not less than 4 M of slats." Support of the amendment can be found throughout the specification, for example, at page 4, lines 7-9 and working examples 1, 2 and 4. In line with the amendment of claims 1 and 11, applicants have cancelled claims 3 and 12. Claims 4 and 13 have been rewritten to depend from claims 1 and 11, respectively, in view of cancellation of claims 3 and 12. Claims 9 and 10 have been amended to clarify that the recitation of "lysis of RNA" refers to "hydrolysis of RNA," as suggested by the examiner.

Response to the Restriction Requirement

The examiner has requested applicants to elect one group between Groups I and II. Applicants confirm the provisional election of Group I made by telephone on July 23, 2002, and cancel claim 15 accordingly. Of course, applicants reserve a right to file a divisional application for the subject matter of claim 15.

New Grounds of Rejection: Rejection of claims 1-14 under 35 U.S.C. § 103

The examiner has rejected claims 1, 2 and 6-11 as allegedly obvious over U.S. Patent No. 5,625,053 to Kresheck *et al.* ("Kresheck") in view of Pentecost *et al.* ("Pentecost"). The examiner has further rejected claims 1-14 as allegedly obvious over

Kresheck and further in view of Puig et al. ("Puig"). Applicants respectfully traverse these rejections.

The claimed invention provides a method for obtaining DNA from fish spermatogonium. It is a general understanding that fish spermatogonium that falls under a mammalian cell does not naturally contain a plasmid DNA. Therefore, it is apparent that the claimed method is directed to isolating a genomic DNA of fish spermatogonium

In contrast, the teachings of Kresheck are limited to a method of isolating a plasmid DNA, not a genomic DNA. Because a supercoiled plasmid DNA does not exist as bound to a protein, there is no teaching or suggestion of using acylation reaction in Kresheck.

Furthermore, Kresheck does not teach or suggest the use of an alkaline solution containing high concentration of salts, i.e., not less than 4 M of salts as claimed in amended claims 1 and 11. While recognizing drawbacks of the existing methods for isolating a plasmid DNA, Kresheck discloses a method that does not involve the recognized problems by using an alkyldimethylphosphin oxide (APO) detergent. The existing methods for isolating a plasmid DNA have used a detergent such as SDS in an alkaline solution to dissolve a cell wall, releasing the chromosomal and plasmid DNAs. Kresheck, therefore, teaches a selection of APO as the detergent essentially required in the existing methods. However, there is no recognition in Kresheck that an alkaline solution with high concentration of salts can perform cell lysis as an alkaline solution with a detergent does, while avoiding drawbacks recognized in the existing methods. As a result, Kresheck provides no suggestion or motivation for one of ordinary skill in the art to use high concentration of salts, i.e., not less than 4 M of salts in the alkaline solution, as claimed in the amended claims 1 and 11.

Neither Pentecost nor Puig cures such deficiencies of Kresheck. At the outset, Pentecost relates to isolation of RNA, not DNA, from trout testis. It is common understanding that, unlike a genomic DNA, RNA similar to a plasmid DNA is not bound to a protein in a cell. This difference has a significance in that the isolation of RNA does not require a separation of RNA from its binding protein. Therefore, there is no

implication or indication in Pentecost that acylation reaction can be used for isolating RNA. Furthermore, Pentecost is silent about using an alkaline solution containing high concentration of salts. Therefore, Pentecost does not provide any suggestion or motivation that one skilled in the art would have modified the method of Kresheck to use the alkaline solution containing high concentration of salts, and to include acylation reaction, as claimed in the instant case.

In this regard, the examiner attempts to combine the method of Kresheck with the disclosure of Puig to come up with the claimed method using acylation reaction. Puig allegedly discloses the acetylation of the lysine in histone, H4, which weakens the attachment of histone from DNA. Because Puig describes interactions between histone and DNA that consist of the nucleosome together in a cell, the teachings of Puig are only relevant to a genomic DNA that is bound to a DNA binding protein. As discussed above, the teachings of Kresheck are limited to the isolation of a plasmid DNA that is not associated with a protein such as histone or protamine. Thus, the cited references give no indication that one of ordinary skill in the art would have been motivated to use acylation reaction to isolate a plasmid DNA that is not bound to a protein.

In combining references, there must be a suggestion to make the combination and a reasonable expectation that the combination will succeed. Both the suggestion and reasonable expectation must be found within the prior art, and not be gleaned from applicant's disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). In view of the difference in DNAs discussed in Kresheck and Puig, which results in the different methodology for isolation of these DNAs, there is nothing in the cited references that would have suggested to one of ordinary skill in the art that the references should even be combined.

Furthermore, even if there was motivation to combine the references, the combination would not arrive at the claimed method because the prior art fails to suggest the use of the alkaline solution containing high concentration of salts. Accordingly, there is no *prima facie* case of obviousness.

Even if the examiner had established a *prima facie* case, moreover, it would be rebutted by objective evidence of unexpected advantages of the claimed invention. As described in the specification, the claimed method produces DNAs without generating pollutants and without resorting to the use of harmful materials such as phenol. Eliminating the drawbacks of the existing methods by using an alkaline solution containing high concentration of salts, *i.e.*, not less than 4 M of salts, cannot be predicted from the prior art that is silent in this perspective, and would be considered an unexpected advantage of the claimed invention.

The attainment of unexpected results or properties is a powerful demonstrations of patentability. See U.S. v Adams, 383 U.S. 39, 51-52 (1966); Lindemann Maschinenfabrik v. American Hoist and Derrick Co., 730 F.2d 1452, 1461 (Fed. Cir 1984). Applicants' demonstration of unexpected results further establishes patentability of the claimed invention. Accordingly, reconsideration and withdrawal of these obviousness rejections are respectfully requested.

Rejection of Claims 8-10 under 35 U.S.C. §112, second paragraph

The examiner has rejected claims 8-10 as allegedly indefinite due to the recitation of "lysis of RNA." At first, applicants note that claim 8 is not relevant to the objected recitation, and thus understand that this rejection only applies to claims 9 and 10. Without acquiescing to the examiner's position in this rejection, applicants have obviated this rejection by revising the objected recitation to read "hydrolysis of RNA," as suggested by the examiner. Accordingly, applicants respectfully request withdrawal of this rejection.

In view of the foregoing, applicants request favorable reconsideration and allowance of the pending claims. If there are any issues remaining which the examiner believes could be resolved through either a supplemental response or an examiner's amendment, the examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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VERSION SHOWING MARKED UP CHANGES

In the Claims:

In accordance with 37 CFR §1.121, please substitute for original claims 1, 4, 9-11 and 13 the following rewritten versions of the same claims, as amended. The changes are shown explicitly in the attached "Version with Markings to Show Changes Made."

- 1. (Twice Amended) A process for obtaining deoxyribonucleic acid (DNA) from fish spermatogonium, which comprises:
- i) disrupting a fish spermatogonium to produce a milky-white colloid containing DNA;
- ii) adding an alkaline solution of pH 8 to pH 12 that contains [more than 1] not less than 4 M of salts to said milky-white colloid [to separate DNA from protamines];
- <u>iii)</u> <u>effectuating acetylation reaction of a mixture obtained in step ii);</u>
- [iii)] \underline{iv} adding ethanol solution to [the] \underline{a} mixture obtained in step [ii)] \underline{iii} to precipitate DNA.
- 4. (Amended) The process according to claim [3]1, wherein said acylation reaction is performed by using anhydride compounds.
- 9. (Amended) The process according to claim 1, further comprising a step for [lysis] <u>hydrolysis</u> of RNA.
- 10. (Amended) The process according to claim 9, wherein said step for [lysis] <u>hydrolysis</u> of RNA is performed by the alkali or RNase.
- 11. (Twice Amended) A process for obtaining deoxyribonucleic acid(DNA) from fish spermatogonium, which comprises:

- i) disrupting a fish spermatogonium in an alkaline solution of pH 8 to pH 12 that contains [more than 1] not less than 4 M of salts;
- <u>ii)</u> <u>effectuating acylation reaction of a mixture obtained in step i);</u>
- [ii)] \underline{iii} adding ethanol solution to the mixture obtained in step [i)] \underline{ii} to precipitate DNA.
- 13. (Amended) The process according to claim [12] 11, wherein said acylation reaction is performed by using anhydride compounds.